

2010 Annual Report: Embryonic Stem Cells

News at CIRM:

Embryonic Stem Cells Remain the Gold Standard

On August 23 federal judge Royce C. Lamberth ruled federal funding of human embryonic stem cell research impermissible under current laws. This decision suspended the ability of the NIH to fund research using human embryonic stem cells, a result that NIH director Francis Collins likened to pouring sand in the engine of discovery.

By September 9, 2010 the U.S. Court of Appeals put a hold on that ruling, allowing funding to continue, though the outcome of the case is still unknown. With this surprising turn of events, one question kept surfacing: Why do we even need embryonic stem cells when the science of adult stem cells and reprogrammed iPS cells is so advanced?

In the Beginning

"No adult stem cell can ever go on to be another cell type, even one that's closely related."

Irv Weissman,
Stanford University

In 1988, Irv Weissman of Stanford University isolated the first adult stem cells. These were the blood-forming stem cells from the bone marrow of mice. He soon isolated the same cells in humans, and over the following decade he isolated stem cells in additional tissues and started a series of companies dedicated to developing therapies based on those discoveries.

Given that Weissman's reputation and personal income are invested in the future of adult stem cells you'd think he would be their biggest fan. Instead, Weissman, who is now the director of Stanford's Institute for Stem Cell Biology and Regenerative Medicine, is one of the most vocal supporters of funding for embryonic stem cells.

Adult stem cells, or tissue-specific stem cells, reside within the bone marrow, brain, blood, skin, liver or other tissues until disease or injury calls upon them to finish maturing to repair the damage.

"These cells are restricted in what they can do," Weissman said. "No adult stem cell can ever go on to be another cell type, even one that's closely related."

By contrast, embryonic stem cells can form every single cell type in the body. They come from embryos discarded after a couple completes in vitro fertilization treatment, can be frozen or grown indefinitely in the lab and with a bit of coaxing can mature into any desired cell type.

This flexibility is what accounts for much of the therapeutic hope for embryonic stem cells. They've been matured into nervous system precursor cells that are now in clinical trials for spinal cord injury and they can also form structures in the eye that are now being tested as a therapy for two forms of blindness. Other research teams have matured the cells into types that could become therapies for diabetes, skin diseases, heart disease, neuronal diseases or cancer, among others.

By Way of Comparison

A less discussed but equally critical role for embryonic stem cells is as a research tool. Weissman's team has relied on knowledge gained from embryonic stem cells to guide their adult stem cell discoveries. Rather than sifting through mouse tissues looking for adult stem cells, his team matured embryonic stem cells until they reached the adult stem cell stage. They could then use what they'd learned about those stem cells to find the counterparts in actual animal tissues.

James Thomson, one of the first to reprogram skin cells into embryonic-like iPS cells, has said that restrictions on funding for embryonic stem cells set the discovery of reprogrammed iPS cells back by about five years. He wrote in the Dec. 3, 2007 *Washington Post*, "Work by both the U.S. and Japanese teams that reprogrammed skin cells depended entirely on previous embryonic stem cell research."

Creating the initial iPS cells and the newer techniques that followed (See Making a Better iPS Cell) came about, in part, by studying embryonic stem cells to understand what it is that makes a cell able to form all cell types of the body.

Even with improvements in creating iPS cells, there's a lot we still don't know. Paul Knoepfler at the University of California, Davis says there are hints that iPS cells when transplanted are more prone to forming tumors than embryonic stem cells. But then, those studies were done on iPS cells created using an outdated method. How do the newer techniques compare? Nobody will know until they've done the comparisons against embryonic stem cells.

Keeping the Pipeline Full

Adult stem cells were first successfully used in humans in 1968 in the form of a bone marrow transplant (it's the blood-forming stem cells in the bone marrow that rebuild the blood system). Those cells are now in clinical trials for a range of diseases, and adult neural stem cells are just starting to be tested for spinal cord injury and ALS, among other conditions.

To some, the fact that adult stem cell clinical trials have started means embryonic stem cells came along too late. By that logic, cancer patients would still be receiving the very first extremely toxic and only somewhat effective chemotherapies.

Instead, scientists continued testing new ideas as they emerged. Through that clinical trial and error process we now have highly targeted antibody-based cancer therapies as well as more effective standard chemotherapies. This range of therapeutic options would never have been developed if scientists were satisfied with their earliest attempts.

Funding restrictions for embryonic stem cells would mean not only fewer embryonic stem cell-based therapies to be tested, but also fewer adult, cancer, or iPS cell therapies.

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